Molecular Biology

CREATING MOLECULAR TOOLS TO DEVELOP A *SCHIZOSACCHAROMYCES POMBE* MODEL TO STUDY PROTEIN MISFOLDING IN PARKINSON'S DISEASE.

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Parkinson's Disease (PD) is a fatal neurodegenerative disease that causes the patient to exhibit resting tremors, slowness of movement, and postural rigidity. PD causes neuronal cell death in the substantia nigra, an area of the brain responsible for coordinating movement. In PD, α-Synuclein, a protein found in this area, which, when misfolded because of or regardless of mutation, is thought to kill these neurons. The ability to reverse α-synuclein misfolding is therapeutically beneficial. Several model systems, in bacteria, flies, worms and mice, have already provided insight into the misfolding of α-synuclein. Our lab has previously begun modeling α-synuclein misfolding in *Saccharomyces cerevisiae* (in which several neurodegenerative diseases have already been modeled). We also aim to model α-synuclein misfolding in the fission yeast, *Schizosaccharomyces pombe* (in which no neurodegenerative diseases have been modeled) because this yeast shares even closer similarities to human cells. This study's goal is to create molecular tools for a *S. pombe* model that will test these two hypotheses: 1) protein misfolding will be accelerated by increased level of expression; 2) the larger the extent of misfolded protein, the more resistant it will be to degradation. Thus far, we have subcloned wild type and three mutant forms of α-synuclein into a set of three *S. pombe* expression vectors with increasing promoter strengths. All vectors have been transformed into yeast and expression of α-synuclein protein has been verified by Western blotting. Currently, we are testing the first hypothesis with differential centrifugation experiments and the second hypothesis with loss of induction experiments. These experiments will increase our understanding of how α-synuclein misfolds and the development of this model system will assist in the future discovery of protein misfolding regulators.